REMARKS

The present application includes claims 118-134. Claims 126-134 have been withdrawn from further consideration by the Examiner. By this Amendment, claim 118 has been amended and claims 126-134 have been cancelled.

Election/Restriction

In response to the Examiner's restriction/election requirement of January 9, 2007, the Applicants provisionally elected, with traverse, Group 5, the species tumor associated antigen, and the single tumor associated antigen nucleic acid of SEQ ID NO. 19. *See* Applicant's Reply filed on April 4, 2007, page 6. In the present Office Action, the Examiner has made final the restriction/election requirement. Pursuant to 37 C.F.R. § 1.142(b), claims 126-134 have been withdrawn from further consideration without prejudice to the Applicants' right to file one or more divisional or continuing applications.

The present Office Action notes that the sequence identity between the polypeptides of SEQ ID NOs: 22-24 and 58-61 are sufficiently distinct to warrant separate sequence searches and that searching all 7 sequences would entail a serious search burden. June 7, 2007 Office Action, page 2. In response, the Applicants, with respect to claims 118-125, hereby elect a tumor associated antigen selected from the group consisting of: a polypeptide of SEQ ID NO: 22 or a portion thereof; a polypeptide encoded by a nucleic acid of SEQ ID NO: 19 or a portion thereof; and a polypeptide encoded by a nucleic acid that is complementary to a nucleic acid of SEQ ID NO: 19 or a portion thereof. Notwithstanding Applicants' election, claim 124 remains within the scope of the elected

subject matter because it encompasses the method of independent claim 118 and the inclusion of additional tumor-associated antigens in this method in an additive manner.

The Applicants' election is made without prejudice to their right to file one or more divisional applications directed to any non-elected subject matter.

Summary of the Bases for Rejection

Claims 118-125 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly failing to particularly point out and distinctly claim the subject matter which the applicants regard as the invention. Additionally, claims 118-125 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. The Applicants will address each of these bases of rejection in Sections I and II, respectively, which follow.

I. 35 U.S.C. § 112, paragraph 2

The Office Action states that the phrase "'hybridizes to' is indefinite because it is not clear as to the property boundary encompassed by the term." June 7, 2007 Office Action, page 4. Applicants submit that the amendment to claim 118 obviates this part of the rejection.

II. 35 U.S.C. § 112, paragraph 1

The Office Action states that the specification does not enable the claims because "the specification does not provide examples or guidance for diagnosing a disease characterized by expression or abnormal expression of the peptide of SEQ ID NO:22 comprising detecting the peptide from a biological sample isolated from a patient wherein

detection of the peptide in the sample in an amount greater than that of a normal biological sample indicates the disease." June 7, 2007 Office Action, page 6. To the contrary, the specification illustrates the method of diagnosing a disease characterized by expression or abnormal expression of a tumor-associated antigen comprising the detection of a tumor-associated antigen.

For example, as described in one of the embodiments depicted in the specification, detection of the tumor-associated antigen may include: (1) contacting a biological sample with an agent which binds specifically to the tumor-associated antigen; and (2) detecting the formation of a complex between the agent and the tumor-associated antigen. Specification, page 12, lines 14-25. The specification provides a number of well-known methods for creating agents which bind specifically to tumor-associated antigens, including conventional antibody production (page 33, line 12 to page 35, line 11) and phage display (page 35, line 23 to page 36, line 10). The specification also identifies the extracellularly exposed regions of TPTE that are particularly suitable targets for binding substances. Specification, page 63, line 39 to page 64, line 9; SEQ ID NOs: 81-82. Finally, the specification includes non-limiting examples of well-known diagnostic substances for visualizing cells and tissues expressing the tumor-associated antigen. Specification, page 36, lines 12-27.

According to the specification, "the term 'disease' refers to any pathological state in which tumor-associated antigens are expressed or abnormally expressed." Specification, page 37, lines 20-22. The Examiner objects that there are no examples demonstrating that

the peptide of SEQ ID NO: 22 is upregulated in any cancer. However, Example 2 of the present application demonstrates that expression of TPTE mRNA is detectable in several cancer types, but not in normal, non-testis tissue. *See, e.g.*, Specification, page 62; Table 2. The Examiner has noted that "it is well known and recognized in the art that mRNA detection is not an indication of protein production level." June 7, 2007 Office Action, page 7. The Applicants have found, using specific antibodies, that TPTE protein is selectively expressed in testis and in a number of different tumors. Specification, page 63, lines 32-34. Indeed, Applicants have shown that expression of TPTE mRNA is associated with expression of TPTE protein in tumors. *See* Specification, pages 62-64. Moreover, TPTE protein was expressed on the surface of tumor cells, offering the possibility of identification of tumor cells using antibodies against TPTE. Specification page 63, line 39 to page 64, line 9. Thus, expression of TPTE in a biological sample in an amount greater than that in a normal biological sample is indicative of cancer. Thus, Applicants respectfully rebut the Examiner's generalized assertion noted above.

The Examiner also objects to the lack of "a nexus between the disease status of the patient and the expression of the peptide of SEQ ID NO:22." June 7, 2007 Office Action, page 6. The Applicants submit that, in view of the portions of the specification cited above, TPTE is a highly specific biomarker for tumor tissue. The Office Action cites to Tockman et al (Cancer Res., 1992, 52:2711s-2718s) for the proposition that "[t]he essential element of the validation of an early detection marker is the ability to test the marker on clinical material obtained from subjects monitored in advance of clinical cancer and link

those marker results with subsequent histological confirmation of disease." Office Action, page 7; quoting Tockman et al. Tockman appears drawn to biomarkers for *early* lung cancer detection and, particularly appears concerned primarily with population-based screening as opposed to diagnostic (or confirmatory) tests. *See, e.g.*, Tockman et al., page 2713s-2716s. Conversely, the present application is directed to the identification of a highly sensitive and specific biomarker for cancer and does not exclusively concern the early detection of cancer. Since TPTE is not expressed in normal, non-testis tissue, but is expressed in various types of tumor tissue, TPTE qualifies as a highly specific biomarker for cancer tissue.

Moreover, the specification clearly states that TPTE-transfected cells markedly increased cellular migration in 4 independent "Boyden chamber" experiments. Specification, page 64, lines 9-17. As the Applicants note, these results indicate that TPTE plays an important part in the metastasizing of tumors. Specification, page 64, lines 17-19. These data strongly suggest that TPTE has a causative function in the development of cancer.

Finally, the Examiner specifically draws attention to Claim 125 and states that "[t]he specification does not provide any examples of any peptides that are complexed with an MHC molecule and induce an immune response." June 7, 2007 Office Action, page 8. Applicants respectfully submit that claim 125 is directed to a method of diagnosing a disease comprising detection of a tumor-associated antigen in a complex with an MHC 1 molecule. Figure 13 (page 113) depicts MCF-7 cells that were transiently transfected with

a TPTE expression plasmid. The specification further reports that "[t]he antigen ... showed *distinct colocalization with MHC I molecules located on the cell surface.*" Specification, page 52, lines 29-31. Moreover, the specification contemplates an antibody for detecting TPTE that may bind selectively to a complex of (i) TPTE and (ii) an MHC molecule, without binding to either molecule alone. Specification, page 19, line 39 to page 20, line 6. Thus, the instant specification provides examples of TPTE peptide complexed with an MHC molecule.

CONCLUSION

In accordance with the Remarks provided above, Applicants elect a tumor associated antigen selected from the group consisting of: a polypeptide of SEQ ID NO: 22 or a portion thereof; a polypeptide encoded by a nucleic acid of SEQ ID NO: 19 or a portion thereof; and a polypeptide encoded by a nucleic acid that is complementary to a nucleic acid of SEQ ID NO: 19 or a portion thereof. Applicants' election is made without prejudice to their right to file one or more divisional applications directed to any non-elected subject matter. Furthermore, for all of the above reasons, Applicants submit that the specification enables the full scope of the claims, and reconsideration of the Examiner's rejection is respectfully requested.

Applicants believe that a fee of $ 460.00 is due in conjunction with the two month Petition for Extension of Time submitted herewith. The Commissioner is authorized to charge the $460.00 fee, along with any additional fees that may be necessary, or credit any

overpayment, to the Deposit Account of McAndrews, Held & Malloy, Account No. 13-0017, with regard to this Amendment and Response.

Respectfully submitted,

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